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Scanning capillary microscopy: new achievements and opportunities

I.V. Yaminsky

Lomonosov Moscow State University, 119991, Moscow, Russian Federation
yaminsky@nanoscopy.ru
Advanced Technologies Center, 119311, Moscow, Russian Federation
Energy Efficient Technologies, 119234, Moscow, Russian Federation

Scanning probe microscopy has proven to be an effective tool for visualizing biomacromolecules, bacteria, living cells and tissues in the natural environment with unprecedented spatial resolution. Scanning probe microscopy makes successful steps in the development of molecular diagnostic methods for personalized medicine, in particular, for the early detection of biological agents and markers of various diseases. Methods of scanning probe microscopy demonstrated the detection of a bacterium, a virus [1], a protein, and even a single atom [2]. An effective method for the rapid detection of bacterial resistance to antibiotics was developed and demonstrated in [3]. Highly sensitive detection of viral particles at low concentrations in liquid solutions was shown in [4].

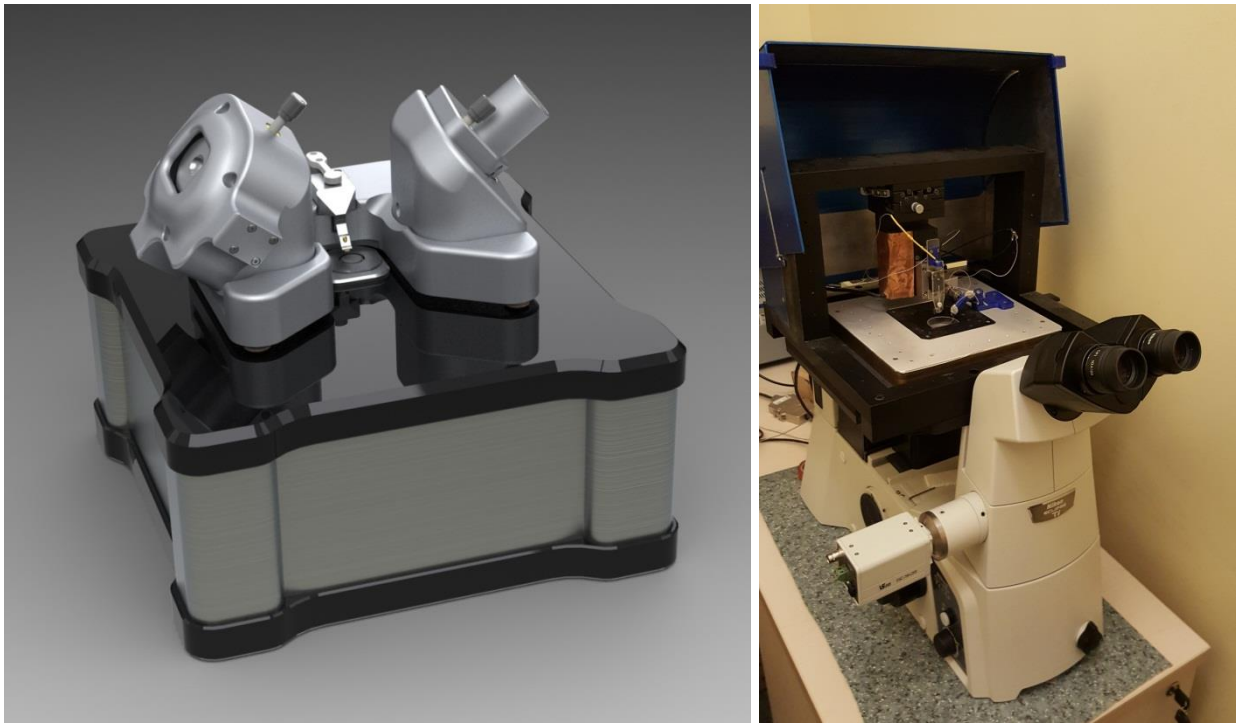

Figure 1. FemtoScan X high-speed scanning probe microscope (left) and scanning capillary microscope combined with Nikon Ti- U inverted optical microscope (right).

Modern scanning capillary microscopy plays a crucial role in various biomedical applications. A capillary probe or a nanopipette of a scanning capillary microscope can act as a device for delivering drugs, an electrochemical sensor, a pH biosensor, a test system for detecting metal ions and many others. Capillaries with two or more channels also allow the directed mass transfer of substances, biomacromolecules (peptides, proteins, nucleic acids, etc.) to the surface of biological objects or inside their volume. In our studies, we use a device embedded in an inverted microscope, so that data from optical and probe microscopy can be obtained and analyzed simultaneously [5]. For example, erythrocytes were observed using a scanning capillary microscope, and an analysis of the results showed that their surface roughness was in the range of 20 nm [6]. In this paper, we use the term “capillary microscopy” because it combines much more functions and methods of use compared to the name “scanning ion-conducting microscopy (SIPM)”, which has traditionally been used previously. Scanning capillary microscopy is successfully developing due to the effective use of multichannel capillaries for directional surface modification and 3D printing. It is possible to predict the further widespread use of scanning capillary microscopy in biomedical applications, in the testing of drugs using only one cell, and

not their cultures. A promising application of capillary microscopy is stereolithography. Art print using fluorescent proteins was first demonstrated in [7]. This work opens up new unique opportunities for the use of multi-channel capillaries for various technological and biomedical applications. The present and future of scanning capillary microscopy for 3D printing and stereolithography is the subject of discussion.

Modern scanning probe microscopy continues to grow rapidly. An important modern trend is to increase the speed and amount of data. Many scientific groups and companies are successfully working in this direction. At present, we have implemented a data acquisition system based on 18-20 bit DACs and ADCs at an operating frequency of 1 MHz. In this case, a frame with a size of 1000x1000 points is taken in 1 sec. However, this is far from the limit for probe microscopy. We are currently developing multichannel electronic data acquisition systems operating at a frequency of 100 MHz – 1 GHz.

Combined techniques are successfully developed when scanning probe microscopy is used with ultra-high-resolution optical microscopy, optical tweezers, optical spectroscopy, etc. Chemical analysis of the surface by recording the absorption of infrared radiation using a probe microscope are one of new techniques. In this method, one can distinguish chemically inhomogeneous areas in biological objects with a resolution of up to 10 nm [8].

Software plays an important role in the development of scanning probe It allows not only to obtain data, but what is very important, to efficiently and effectively process data, to present it in a visual and convenient form. These functions are largely performed by the FemtoScan Online software [9,10]. The FemtoScan Online software integrates the reading of files from most manufacturers of scanning probe microscopes. The development of probe microscopy occurred in such a way that almost all microscope developers used their unique recording data formats, which are implemented into FemtoScan Online software.

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